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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,497	09/08/2006	Randall T. Peterson	00786/443002	8998

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EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
08/20/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/564,497	PETERSON ET AL.	
	Examiner	Art Unit	
	GREGG POLANSKY	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *3-5 and 8-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 January 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/12/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicants' preliminary amendments, filed 1/12/2006, amending Claim 16, adding Claims 18-21, and adding a priority claim to the Specification, are acknowledged.

2. Applicants' Information Disclosure Statement, filed 1/12/2006, is acknowledged and has been reviewed to the extent that each is a proper citation on a U.S. Patent. The international search report from PCT/US04/20893 is not a proper citation and has not been considered.

3. Applicant's election without traverse of Group I (Claims 1-9) and species GS4012 and treating myocardial ischemia, in the reply filed on 4/07/2008 is acknowledged. The Restriction Requirement is thus deemed to be proper and is made Final.

4. Claims 1-21 are pending.

5. In accordance with 37 CFR 1.142(b), Claims 10-21 are withdrawn from consideration because they are contained in non-elected groups, and Claims 3-5, 8 and 9 are withdrawn from consideration because they are not drawn to the elected species.

6. Claims 1, 2, 6, and 7 are presently under consideration.

Specification

The disclosure is objected to because of the following: On page 3, the 2nd paragraph discloses that "[i]n formula(I), Y is selected from CH_2, $C(CH_3)$, CH_2CH_2, $CH_2CH_2CH_2$, $CH_2CH{=}CH$, and **$CH_2CH\ \ C$**" (emphasis added). It is not clear what "$CH_2CH\ \ C$" represents or how it can be incorporated in formula(I).

Appropriate correction is required.

Drawings

7. The drawings are objected to because Figures 1A, 1B, 3B, and 3C are not readable. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 2, 6, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites that Y of formula (I) "is selected from CH_2, $C(CH_3)$, CH_2CH_2, $CH_2CH_2CH_2$, $CH_2CH{=}CH$, and **CH_2CH C**" (emphasis added). It is not clear what "CH_2CH C" represents or how it can be incorporated in formula(I).

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 2, 6, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the Specification does not reasonably provide enablement for preventing or treating vascular diseases. The Specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

Claim 1 is drawn to a method of treating or preventing vascular disease or promoting vascular growth or development in a patient. Claim 6, which depends from Claim 1, is drawn to said patient having or at risk of developing ischemia. Claim 7 further limits the ischemia to myocardial, cerebral, mesenteric, or limb ischemia, caused by a wound, vascular occlusion, or vascular stenosis; or said patient has suffered or is at risk of suffering a heart attack or stroke. Claim 1 does not define the type or etiology of the vascular disease, and thus fails to define a population for treatment for the disease. The instant Specification defines "prevent" as the "prophylactic treatment of a human patient who is not yet ill, but who is susceptible to, or otherwise at risk of" a disease. The Specification provides no teaching of the process of identifying a patient at risk of developing vascular disease.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The document, "What is vascular disease?", published online by the Cleveland Clinic (http://my.clevelandclinic.org/heart/disorders/vascular/whatis.aspx, downloaded 8/08/2008) teaches vascular disease includes any condition that affects the circulatory system, "ranging from diseases of [the] arteries, veins and lymph vessels to blood disorders that affect circulation". See page 1, 2nd paragraph. The reference teaches atherosclerosis in coronary and peripheral arteries causes ischemia in the tissues being supplied by the arteries (coronary and peripheral artery disease). Other vascular diseases include aneurysm, Raynaud's disease, Buerger's disease, peripheral venous

disease, varicose veins, blood clots and blood clotting disorders, pulmonary embolism, chronic venous insufficiency, and lymphedema. See pages 1-4. The document "Vascular Diseases", published online by MedlinePlus (http://www.nlm.nih.gov/medlineplus/vasculardiseases.html, 7/27/2008, downloaded 8/08/2008) teaches factors that increase the likelihood of developing vascular disease include a family history of vascular or heart diseases, pregnancy, illness or injury, smoking, obesity, "any conditions that affects the heart and blood vessels, such as diabetes or high cholesterol", and long periods of sitting or standing still. See page 1.

Thus, it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "preventive" effect. Further, one of skill in the art would not expect a single compound to be effective in treating all vascular diseases, or even all ischemic vascular diseases.

(5) The relative skill of those in the art:

The relative skill of those in the art of cardiovascular medicine or pharmacology and the unpredictability of the pharmacy art is very high. In fact, the courts have made a distinction between mechanical elements, which function the same in different circumstances, yielding predictable results, and chemical and biological compounds, which often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is

considered to be an unpredictable art. Likewise, the physiological or pharmaceutical activity of treating or preventing vascular diseases, especially an undefined vascular disease or a defined vascular disease with undefined etiology, is an unpredictable art.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The Specification teaches stimulation of angiogenesis and vasculogenesis to aid "the healing of wounds, the vascularizing of grafts (e.g., skin grafts), and the enhancement of collateral circulation (e.g., in cases of vascular occlusion or stenosis)", and that stimulation of these processes can be beneficial in treating or preventing ischemia. See page 2, 1st paragraph. The Specification alleges that administration of the disclosed compounds is effective for treating or preventing vascular diseases or promoting vascular growth or development in patients. The Specification teaches that the zebrafish mutation, *gridlock*, "disrupts the bifurcation of the aorta, blocking distal blood flow in a region and physiological manner akin to aortic coarctation in humans". See page 18, last paragraph. The Specification provides experimental data alleging the disclosed compounds, gs4012 and gs3999, possess *gridlock* suppressor activity. See Figures 1C and 1D. The Specification provides data alleging to demonstrate the effectiveness of the disclosed compounds at suppressing *gridlock* in angioblasts of zebrafish during the early stages of embryonic development. See page 20. The Specification has provided guidance for identifying a patient at risk of ischemia in patients contemplating surgery.

However, the Specification provides no guidance or experimental results demonstrating the effectiveness of administration of the disclosed compounds in

(8) The quantity of experimentation necessary:

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fishcher, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a Specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. As discussed above, considering above factors, especially the "sufficient working examples", "the level of skill in the art", "the relative skill and the unpredictability in the pharmaceutical art", "breadth of the claims" and "the chemical nature of the invention", one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the claimed compounds for the claimed methods of prevention or treatment of vascular diseases.

12. Claims 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, as lacking a clear written description of the invention and of the manner and process of practicing it, in such full, clear, concise and exact terms as to enable any person skilled in the art to

which it pertains, or with which is most nearly connected, to practice same, and, as not setting forth the best mode contemplated by the inventor to carry out the invention.

Claim 6 is directed the patient of Claim 1, wherein said patient has or "is at risk" of developing ischemia. Further, Claim 7 is drawn to the patient of Claim 6 who has suffered or "is at risk" of suffering a heart attack or stroke. One skilled in the art finds no guidance with respect to identifying or treating patients at risk of developing ischemia or suffering a heart attack or stroke. There is no showing that Applicants had possession of the claimed invention in this regard.

Conclusion

13. Claims 1, 2, 6, and 7 are rejected.

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1611

/Ardin Marschel/
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